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Thank you Lord Taverne, and Professor Stott in particular for the opportunity to address this audience today. On behalf of my colleagues at Dupont, in general, and specifically Protein Technologies International, I welcome the opportunity to come and participate in this forum. We have had the pleasure to host a number of delegations from the United Kingdom at our facilities in the United States, so we welcome the opportunity to reciprocate and participate in the discussion here today.

My presentation has three portions. The first is a list of general categories of consumer and environmental benefits upon which our company and others are working. The second portion will characterize the general techniques and types of tools that we use to create and develop the new products that deliver these benefits. Dr. Dale did a good job this morning describing these. I won't spend too much time here other than to emphasize that we use an integrated toolbox, including conventional and modern biotechnology. The final portion of my presentation will show you some specific examples of projects at DuPont that use conventional and modern biotechnology to create products that have the potential for consumer benefits.

So with that as an introduction, we will start with this list of opportunities to deliver consumer benefits. First and foremost is the ability to enhance and improve the quality of the basic components of crop plants, e.g., the proteins, oils, carbohydrates and bioactive components are all at hand now. In particular we are looking at opportunities to create stable (i.e., from a flavor standpoint); healthier oils that can even help reduce or even eliminate the need for chemically hydrogenated fats. As an example, I was walking near the university yesterday and there was an organic food café and very clearly on the window was a sign that saying that none of their products contained hydrogenated fats. They are like many members of the food industry that are trying to provide products with reduced amounts of saturated and hydrogenated fats.

Stable oils also provide us with an opportunity to use them as a base stock for environmentally friendly lubricants. These lubricants are safer, less toxic, and less flammable compared to lubricants made from petroleum. Grain crops like corn, soy and other cereals contain a number of anti-nutritional compounds. We are discovering that biotechnology can be used to reduce or eliminate these anti-nutritionals. This may allow us to better use whole grain products and get the benefit of whole grain products compared to what we are doing today. A related opportunity is reducing the environmental waste produced during animal production. In particular, phosphorous pollution is something that we will talk about. New grains

produced using biotechnology can be used to improve the quality of the dairy, meat and egg products that are produced by feeding these grains. Another opportunity is to use biotechnology to produce the grain based raw materials for making refined protein and oil ingredients that deliver health benefits. Specifically, the combination of oils and proteins with bioactive components that deliver health benefits is a very rich opportunity to impact a number of the major diseases that affect our population, and we will talk about this in a few minutes. Finally from a longer-term perspective, modern biotechnology is capable of improving the basic nutrition, as well as the functional performance of ingredients. These functional properties include features such as taste, texture and color.

The perspective that we bring to the world as its largest supplier of isolated soy protein is that we face a serious challenge to meet the current and especially the future needs for quality protein. You hear discussions that the world doesn't need more food, rather they need a better system to distribute it. There is little doubt that food distribution is a serious issue that needs to be addressed. However, from a protein quality stand point, global supply is still a major limitation and will continue to get worse as world population increases and we reach the limits of arable land. This is a very serious issue as we go forward in time. Much of the future population growth will occur in areas of the world where the infrastructure for the production and processing of animal proteins is very limited. The population in many of these areas is also lactose intolerant, particularly sub-Saharan Africa. From a quantitative perspective, for each additional billion mouths that we add to the planet, we need to provide about 32 billion pounds annually of quality protein, just to meet those bare minimum requirements set by the FAO/WHO. As a planet we are doing this at a rate of 1 billion people every 12 to 13 years.

It is key that this protein is of a high quality. The protein needs to be a balanced protein that meets the essential amino acid requirements for human nutrition. Today's typical North American and Western European diet contains about twice those protein levels. As a result, you need about 60 to 65 billion pounds of protein to meet those needs of those billion additional mouths. This quantity of protein is equivalent to all of the soybeans produced in the United States today; we produce about 65 billion pounds of protein. The vast majority of that, almost 95% to 97%, goes into animal production and therefore is not directly consumed by humans. So there is an environmental component to nutrition in that if every 10 to 12 years we are adding another billion people to the planet or we have a billion people that are trying to increase their nutritional standard of living and move towards a higher quality diet then somewhere, somehow, we have to come up with the equivalent of about 70 million acres of soybean production.

Now from our perspective in the United States that's about two thirds of all the land we set aside for the national wildlife reserves and it's about the entire landmass of the United Kingdom. So, every 12 years we have got to come up with that equivalent production unless we find a different way of either consuming food or being much more efficient, particularly around protein.

Protein quality is critical from vegetable sources; most of the cereals and a number of the legumes are not as nutritious from an amino acid digestibility standpoint as is soy protein. This table simply shows you for comparison purposes that soy protein when processed properly has a protein digestibility amino acid score (PDCAAS) equivalent to milk, meat and eggs. In contrast to this, other legumes and cereal products, particularly wheat and especially wheat gluten, are far inferior in terms of their ability to supply essential amino acid nutrients. Those essential nutrients are very critical in growth and brain development and a number of other critical factors in the development of our infants.

If you ignore for a second just the basic need to supply amino acids and proteins and calories, we still have a number of major quality factors related to our diets that influence our society's health. We focus our efforts heavily on cardiovascular health, as cardiovascular disease is a leading cause of death in the US, EU and Canada. About half of our audience here today is at risk due to their high serum cholesterol content, and one in five of us is at major risk with greater than 240 milligrams per deciliter of cholesterol. One in three women in the audience will experience cardiovascular disease. In women, the first incidence of cardiovascular disease is typically much more severe than it is in men, and is often fatal. Poor diet is a major risk factor associated with cardiovascular disease. Both saturated fat and *trans* fats are the fats that are produced during the chemical processing of vegetable oils. Intake of both should be limited in order to manage the serum cholesterol and other lipids that are associated with cardiovascular disease. The key benefit from a reduction in serum cholesterol is that for every 1% reduction in cholesterol we get a 2% to 3% reduction in cardiovascular disease. So there is an enormous personal and societal benefit from being able to do that and do it in a convenient way from ingredients in one's diet. There is increased consumer awareness of the link between various components of our diet and disease, as well as the use of diet as another tool to help manage our overall health. The use of diet as a tool versus drugs, for instance, is now increasingly favored by many people in the EU. In the United States we have a number of initiatives that are underway by the FDA or have been enacted. Oat bran and beta glucan use in managing cholesterol is one example. Recently, the FDA has granted a health plan for the

consumption of soy protein, when consumed as part of a low fat, low sodium diet. They also have a rule pending in 2004, which will require the mandatory labeling of the *trans* fatty acid content in foods.

Another area of benefits associated with our diet includes women's health. Osteoporosis is a major health factor in the United States as one in two women over the age of 60 will be exposed to this debilitating disease. There is some very encouraging evidence that products like soy protein with naturally bioactive components may be an effective tool in helping manage osteoporosis. A number of cancers are critical diseases as well, and they are the second leading cause of death in men in the US; second only to cardiovascular disease. Other cancers that are important as well include prostate and colon cancer and again soy protein products are showing some promise there. About one in eight American women will be exposed to the threat of breast cancer, and there is evidence that increased consumption of soy products could help. Recently an epidemiological study in Sweden has shown that there may some very positive associations between diets that are high in monounsaturated fats, i.e. oleic acid, and reduced incidence of breast cancer.

General mineral nutrition in developing countries is often an issue, particularly in those regions of the world that consume diets that are heavily corn-based. Corn and soy contain phytic acid, a naturally occurring source of phosphorous that binds certain minerals in one's diet. If one's diet is at all deficient in certain key minerals like iron and zinc, then phytic acid can limit the availability of those important nutrients. Phytic acid has other negative implications that are related to the impact of animal nutrition on the environment and this will be discussed later.

A number of other diet related opportunities are possibilities, but due to limitations in time they will just be mentioned briefly. These include opportunities to manage rheumatoid arthritis and other anti-inflammatory diseases with desirable oils. Another important area of opportunity includes improved cognitive function, not only for infants and the development of critical brain and nerve function but also in managing cognitive function (e.g., dementia and Alzheimer's) in the elderly.

We'll go now to describing the types of tools we are trying to use to deliver these benefits. It is critical that not only the products are able to deliver those benefits but also the tools used to create them are effective and efficient. The message I want to get across to you today from this particular slide is that we err when we evaluate these tools in isolation. We'll often look at conventional biotechnology, modern GM biotechnology or grain processing in isolation. That's simply not the way that we are using the technology. This

slide simply shows that we use all three of these as integrated tools that are most effective when they are used in combination. The term we use for the integrated use of these technologies is a "technology toolbox". Numerous scientific competencies are used in the process of taking a new idea for a healthy product and developing the grain based raw materials and manufacturing processes needed to deliver it safely and efficiently to our diets. We rely heavily on identifying the targets for making new products through use of consumer research and monitoring emerging trends in nutritional science.

Why we use these particular tools is shown in the next couple of slides. Conventional biotechnology as a tool can be quite effective. We've used it to create traits that soybean and maize currently don't possess. The potential for stacking of multiple traits together to deliver multiple benefits is present with both conventional biotechnology as well as modern biotechnology. As Dr Dale indicated this morning it has widespread use in the plant breeding community and a long history of effective and safe use in creating plant varieties. It can, however, be inefficient and costly to identify new sources of variation so we use conventional as well as modern biotechnology to try to create those traits that the grain crops currently don't possess, and that are targets for delivering consumer benefits. We can do things via modern biotechnology that are much more precise, much more selective in expressing these traits within certain parts of the plant that we cannot always do by conventional biotechnology. The biggest benefit, however, is one that is rarely seen by the consumer. When you are trying to stack multiple traits within a single variety, modern biotechnology can be dramatically more efficient than conventional biotechnology. So when we need a trait for a new protein and a new lipid and a new carbohydrate and you have to do that in the same variety, modern biotechnology has the potential to be much more effective and efficient in doing that than conventional biotechnology.

I now want to show you three basic examples, in the time we have remaining. These will be examples where we have used both conventional and modern biotechnology discovery techniques. This first example includes a number of new soybean oils that have been discovered using these techniques. Soybeans with high oleic oil was the first soybean variety produced in the United States using modern biotechnology with a unique oil profile. From its inception we tried to create it with the potential for consumer benefits in mind. We used the techniques of both conventional and modern biotechnology, but we were only successful using modern biotechnology. The oil profile of high oleic varieties discovered using conventional biotechnology was always inconsistent when grown in different environments. However using modern biotechnology we now have high oleic

varieties that have over three times the level of oleic acid oil than commodity soybeans. We have also been able to make soybean oils that are much more stable by reducing the level of polyunsaturated fatty acids. These are the oils that go bad and rancid when they are used in cooking. For this reason the edible cooking oil industry uses chemical processing (i.e., hydrogenation) to create stable oils. You can do that now within the seed and can see the dramatic reduction in the polyunsaturated fat content compared to that of commodity varieties. There are other foods where you want oil with a high saturated fat. Most of us don't like to pour oil onto our food. Instead we like to be able spread it and like it to melt properly in order to taste good. High saturated fats are very useful in a number of baking and confectionery applications. However you want to be able to do that and still minimize the dietary exposure to saturated and *trans* fatty acids as much as possible. We have been able to significantly increase the saturated fat content by a combination of conventional and modern biotechnology. Conversely, we have also been able to do that for liquid oils where we want very low saturated fat content and have used conventional biotechnology to achieve that.

Flavor stability is one of the key issues for vegetable oils, including soy oil. By controlling a soy specific gene we have been able to increase the oleic acid content, and as this slide shows we dramatically improved the flavor stability of the soybean oil produced from that variety. It is very high in monounsaturated fat, higher even than olive oil, it has about a third less saturated fat than regular soybean oil, so it has the potential for helping reduce dietary exposure to saturated fat. As a result, it has very high oxidative stability without any *trans* fatty acids. There is no need for chemical hydrogenation in a number of applications. And, as mentioned previously, it was the first soybean produced by biotechnology with a change in compositional profile that has gone through the regulatory process used by the USDA and the FDA. The consumer benefits here are improved flavor stability, and increased potential for heart and cancer health benefits. Also the potential for environmental benefits exist, because its increased oxidative stability allows high oleic oil to be used as a base oil for environmental lubricants.

I show you this slide really as a good example of how the combination of conventional and modern biotechnology can be very synergistic. When we manufacture vegetable oil spreads (e.g., margarines) today, they need a very specific type of melting profile. We don't want them too liquid because they don't taste good. We don't want them to be too solid, as they will then taste waxy. This slide shows a melting curve for commercial soft tub margarines. The blue lines are commercial margarines that have been produced using chemical hydrogenation. This melting curve is from oil

produced from a non-genetically modified, high stearic acid soybean. It is less solid across the temperature range than the commercial margarines and it therefore does not have the right texture. Oil from high oleic soybean is a liquid throughout the temperature range so it would be even less solid than the high stearic oil. In contrast to these oils, the combination of modern and conventional biotechnology results in the creation of a high stearic / high oleic soybean oil. It has the right fatty acid profile to match the melting specifications of the commercial, high *trans* containing soft tub margarines. The oil from the high stearic/high oleic soybean would not contain any trans fatty acids. This is just one example of a number of market development activities that we have underway with high oleic soybeans. They include a number of food applications, and we are also looking at a number of biodegradable lubricant applications in the United States.

The next example of a new type of grain we are developing is grain with reduced phytic acid to improve the environmental impact of animal agriculture. Phosphorous pollution from animal agriculture is a major issue in the United States and there are some similar concerns in Europe. In the United States these phosphorous pollution hot spots are primarily associated with pork production and broiler production. The principle source of phosphorus pollution is the phytic acid that is present in the animal feed. Phytic acid is a naturally occurring phosphorous source within grains; maize, soy, even the cereals contain it. Animals can't use it because it is in a form that is not biologically available. As a result, it passes through in the manure into the environment. This is an example of how our production of food has a significant environmental impact. The EU faces similar issues in the areas where the density of animal agriculture is high, including many areas in the UK. There is an unmet need for developing grains that can provide the phosphorus needed for animal production in a form that is biologically available. One approach is to develop feed grains and soybean meal with reduced phytic acid.

Soybeans make phytic acid and another family of anti-nutritional sugars, the raffinose saccharides, during the development of the seed. These naturally occurring compounds are made from sucrose that is imported into the seed. These sugars are the sugars that are commonly found in a number of legumes and are poorly metabolized by monogastric animals, including humans. One of the enzymes in the pathway for making these compounds, myo-inositol 1-phosphate synthase, or MIPS, sits at a key branch point between the production of these two types of anti-nutritional compounds. Using conventional biotechnology, we have discovered a mutant that has significantly reduced levels of both phytic acid and the raffinose saccharides. Using the techniques of modern biotechnology we now understand that the MIPS enzyme from the mutant differs from its wild type by a single amino

acid. That minor change in DNA results in an amino acid change in that particular enzyme from a lysine to a glutamine and this change results in a 50% reduction in phytic acid. This reduction in phytic acid results in a tenfold increase in the available phosphorous to the animals, as well as a decrease by over 90% of the poorly digested raffinose saccharides. In addition, the content of sucrose, a sugar that is highly digestible, is approximately doubled in the mutant. Collectively the results indicate how important a change in even a single nucleotide out of millions of base pairs of DNA can be for improving grain quality. This change results in an improvement in the metabolizable energy for monogastric animals, including humans. From an environmental standpoint, animal feeding trials, conducted collaboratively with universities in the U.S., have shown low phytate soybean meal, particularly when fed in combination with high available phosphorous maize can reduce phosphorous excretion into the environment by about two thirds compared to feed ingredients from commodity grains.

Finally, there is a lot of discussion and debate in the scientific and popular press about the potential role of modern biotechnology to increase the amount of allergens. While this is an important food safety issue that must be addressed with any new food, I want to show you another example of just the opposite: modern biotechnology can be used to reduce allergen content. Soy is relatively low in its allergenicity compared to a number of other protein sources, such as milk, eggs, peanuts, fish and crustaceans. Nevertheless, some people are very sensitive to soy. One of the major allergens in soy is called P34; about 90% of the people who are allergic to soy are allergic to it. Expensive processing methods have to be used to remove it from soy protein products and, as a result, are typically not used. Modern biotechnology now allows us to have an additional tool to reduce the level of this allergen that we have not had in the past. P34 has been cloned and its expression has been suppressed in a seed specific manner using modern biotechnology. The last slide shows how the level of P34 protein and the IgE response from a soy sensitive patient have been dramatically reduced with this new soybean compared to the response seen with a conventional soybean. While P34 is a major soy allergen, there are other allergens in soy. We can also reduce their content by modern biotechnology, and by breeding lines with these characteristics, one could eliminate many of the major sources of soy allergy.

So, that's my last slide and I am out of time. Again I have tried to give a perspective of both the tools and the techniques and the general approaches that we are taking in using these new tools to develop products with consumer and environmental benefits. I look forward to the ongoing discussions and again we thank the organizers of the conference for the opportunity to come and speak to the audience.



